



## Mission Slimpossible, Part 3: Tirzepatide for weight loss

### CLINICAL QUESTION

### Is tirzepatide effective for weight loss?

### BOTTOM LINE

**Tirzepatide 10-15mg/week results in ~15-20% weight loss versus 3% placebo at 72 weeks. Most patients on tirzepatide lose at least 10% body weight (78-84% versus ~20% placebo). Weight regain occurs when medication stopped. More weight loss occurs with tirzepatide versus semaglutide (~20% versus ~14%) based on one open-label, tirzepatide-sponsored randomized controlled trial (RCT).**

### EVIDENCE

- All results statistically significant unless indicated.
- Four industry-run, placebo-controlled RCTs:<sup>1-4</sup> Tirzepatide 10-15mg subcutaneous weekly. Baseline weight: 101-107kg. All patients received lifestyle. Excluded: Diabetic retinopathy, macular edema, unstable thyroid disease.<sup>1-3</sup>
  - 2539 without diabetes.<sup>1</sup> At 72 weeks:
    - Mean weight loss: ~20% versus 3% placebo.
    - Proportion who lost  $\geq 10\%$  weight: 78-84% versus 19% (placebo), number needed to treat (NNT)=2.

- Stopping for adverse effects (mostly gastrointestinal): ~7% versus 3% (placebo), number needed to harm (NNH)=25
  - Alopecia (~5% versus 0.9% placebo, NNH=25), dizziness (~4% versus 2.3% placebo, NNH=59)
- 579 without diabetes.<sup>2</sup> Randomized following lifestyle intervention. At 72 weeks,
  - Weight loss 18% (21.5kg) versus 2.5% (3.5kg) gain (placebo).
  - Stopping for adverse events: 11% versus 2% (placebo).
- 938 with diabetes.<sup>3</sup> At 72 weeks:
  - Weight loss: 13-15% (13-15kg) versus 3% (placebo: 3kg).
  - Lost ≥10% weight: 61-65% versus 9% (placebo), NNT=2.
  - Stopping for adverse effects (mostly gastrointestinal): 4% (10mg), 7% (15mg), 4% (placebo).
- Withdrawal RCT.<sup>4</sup> 670 without diabetes. Tirzepatide for 36 weeks then randomized to continue tirzepatide or placebo. After additional 52 weeks:
  - Weight change: 6% loss (tirzepatide) versus 14% gain (placebo).
- Two head-to-head, tirzepatide-sponsored RCTs:<sup>5,6</sup>
  - 751 without diabetes.<sup>5</sup> Open-label tirzepatide 10-15mg versus semaglutide 1.7-2.4mg weekly. At 72 weeks,
    - Weight loss: 20% (23kg) tirzepatide versus 14% (15kg) semaglutide
    - Lost ≥10% weight: 82% versus 61% semaglutide, NNT=5.
    - Stopping for gastrointestinal adverse effects: 2.7% versus 5.6% semaglutide.
  - Other RCT uninterpretable [suboptimal semaglutide dosing (1mg)].<sup>6</sup>

## CONTEXT

- Tirzepatide is approved for weight loss in Canada.<sup>7</sup>
- GLP-1 receptor agonists: Associated with pancreatitis, bowel obstruction and gastroparesis (each up to 7-9/1000 patient-years).<sup>8</sup>
- Dosing: 2.5mg weekly, titrate by 2.5mg every 4 weeks.
  - 5mg dose: 15% weight loss.<sup>1</sup>
- Cost (30-day):<sup>9</sup> ~\$450-880.

## REFERENCES

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